## REMARKS

As an initial matter, Applicant thanks the Examiner for withdrawing the prior rejections and entering the previously submitted claim amendments. At this time, Claims 1-3, 5-7 and 17-22 are pending based on the amendments filed on February 9, 2009. No claim is amended in this response. Claims 1-3, 5-7 and 17-22 are listed here in their clean form without markings for convenience.

Reconsideration and allowance of the amended application are respectfully requested in view of facts and reasoning presented below.

Claims patentable under 35 USC 112

Claims 1-3, 5-7 and 17-22 stand rejected under 35 USC 112, second paragraph as being indefinite because the specification does not provide a limiting definition as to what is encompassed by the term "absorption spectral range of the DNA cells." Applicant respectfully requests the Patent Office to withdraw this rejection.

It is well known in the art that different DNA cells may absorb light at different wavelengths or in different wavelength ranges or spectral ranges. As such, the "absorption spectral range of the DNA cells" may vary depending on the properties of the DNA cells of interest. The specification of this application provides certain examples. In Paragraphs [0049]-[0078], the argon ion lasers operating around 515 nm are described as the excitation source for the Cy3 label in a microarray and other samples based on FWM. Paragraphs [00100]-[00108] describe lasers at 632.8 nm (e.g., He-Ni lasers) for detecting dye samples in capillary cells based on FWM.

Therefore, Claims 1-3, 5-7 and 17-22 are patentable under 35 USC 112, second paragraph.

Claims 3 and 20-22 stand rejected under 35 USC 112, second paragraph as being indefinite for reciting "spatial inhomogeniety" because it is contended in the Office Action that the specification does not provide a definition of the term anywhere. This contention, however, is respectfully traversed.

Applicant respectfully directs the Patent Office to the description in Paragraph [0052] which provides the support for "spatial inhomogeniety":

> [0052] Microarrays are probed, excited, scanned and measured by using a novel forward-scattering degenerate four-wave mixing optical setup based on the absorption of the Cy3 label, which has an absorbance maximum near 535 nm. The 514.5 nm line of an argon ion laser is used as the excitation source for the Cy3 label. The resulting signal is sent through a custom designed precision template and detected by a photodiode. During the spatial scanning process, the laser power used is between 2.5 and 5 mW, but not limited to this range. Microarray spots are scanned with the use of a motorized precision actuator in order to achieve automated and reproducible scans. Background optical noise is determined by scanning the blank glass surface between the spots (i.e., the optical blank). No signal is detected on the blank glass surface, assuring that hybridization and washing are performed effectively. Detection sensitivity is excellent and improving continuously. Our preliminary results indicate that laser wave mixing is one of the most sensitive detection techniques for microarray applications. Laser wave mixing also allows intra-spot spatial resolution where one can scan, probe and measure bio/chemical contents "within" a single spot on the microarray. Preliminary intra-spot scanning and probing show inhomogeniety within each spot due to inhomogeniety in manufactured preprinted spots. Our laser probe diameter is 25 μm, and hence, it requires much smaller amount of reagents for detection. The microarray chips we purchased come with a marker spot. The marker spots located in the corners of each sub-grid contain Cy3-labeled control oligonucleotides. We can even distinguish variations in signal intensity that are due to differences in sequence composition of the 70-mer oligonucleotide targets.

Notably, the above paragraphs provides that "Preliminary intra-spot scanning and probing show inhomogeniety within each spot due to inhomogeniety in manufactured preprinted spots."

Therefore, Claims 3 and 20-22 are patentable under 35 USC 112, second paragraph.

Claims patentable under 35 USC 103(a)

Claims 1-3, 5-7 and 17-22 stand rejected under 35 USC 103(a) over Sandstrom in view of Weinberg and further in view of '444 patent to Tong. These claims, however, are distinctly patentable over the combination of the cited prior art.

With respect to Claim 1, the combination of the cited Sandstrom, Weinberg and Tong, fails to disclose Claim 1 under 35 USC 103(a).

For example, the combined teaching of the cited prior art fails to disclose removing a background noise in the measured DFWM signal of the one DNA cell by using a DFWM measurement of a blank area between the one DNA cell and an adjacent DNA cell; and scanning a position of the microarray to place other DNA cells of the microarray in the DFWM system to get respective DFWM signals.

In this regard, the Patent Office fails to point out any specific teaching in any of the cited Sandstrom, Weinberg and Tong on the above features in Claim 1. Under 35 USC 103(a), the Patent Office must provide a prima facie showing.

Applicant recognizes that, the cited Sandstorm describes using "sites" of an array as the "blanks" or "reference sites" and these sites are clearly the array element sites of the array. See, e.g., the probe sites and reference sites as shown in FIG. 6 in the cited Sandstorm. Paragraph [0019] in the cited Sandstorm is quoted below:

> The system may also comprise computer components for receiving, processing, storing, transmitting, and displaying information received from the detector. For example, a computer processor may be used to receive and interpret information received from the detector. Such information may be manipulated in any number of ways. For example, processed data may comprise data obtained from a first location of the microarray mathematically transformed with data obtained from a second location of the microarray. Such processing finds use, for example, to compare results from two or more known locations on the microarray such as two different experimental sites or an experimental site and one or more control sites. Such information may include complex comparisons of multiple reactions sites on the microarray. The processed information may be provided as a single quantitative "result" which minimizes the amount of informative data that needs to be stored and analyzed. Similarly, in still other preferred embodiments, the spatial light modulator and the computer components are associated such that the system is capable of accessing any probe site in the array. Enhanced signal to noise ratios are contemplated in this method of operation. Moreover, this method of operation allows a number of comparisons between probe sites or sets of probe sites to be quickly drawn. For example, this embodiment allows for analysis, including but not limited to: a) simple fluorescence

> read of a particular probe site (no comparing); b) comparisons of a probe site and a reference (i.e., a blank or non-hybridizable site [eliminates background fluorescence and residual excitation light]); c) comparison of a probe site and a purposefully mismatched site (i.e., eliminates background fluorescence, residual excitation light and signal from nonspecific hybridization); d) comparison of a group of identical probe sites with an equal number of reference sites (i.e., enhances the signal to noise ratio, allows for averages of hybridization across many probes sites); e) comparison of a group of identical probe sites with an equal number of identically mismatched sites; f) comparison of a group of identical probe sites with an equal number of differently mismatched sites; g) comparison of a set of characteristic probe sites with an equal number of reference probe sites; h) comparison of a set of characteristic probe sites with an equal number of probe sites with different characteristics (i.e., useful in clinical diagnostics or expression studies); and i) combinations of the above mentioned comparisons, and other comparisons described herein. In some embodiments of the present invention, the system further comprises a computer memory capable of storing processed data received from the processor.

Notably, nothing in the cited Sandstorm discloses "removing a background noise in the measured DFWM signal of the one DNA cell by using a DFWM measurement of a blank area between the one DNA cell and an adjacent DNA cell" in Claim 1.

The recited "blank area between the one DNA cell and an adjacent DNA cell" in Claim 1 is very different from a "reference site" of an array disclosed in the cited Sandstorm in part because recited "blank area between the one DNA cell and an adjacent DNA cell" in Claim 1 does not occupy a full site of an DNA cell of the array and this operation is possible in part because the specific way that the DFWM is implemented in the microarray of DNA cells as provided in Claim 1: placing a single template located between the microarray and an optical detector to include holes arranged to selectively transmit the DFWM signal from the microarray to the optical detector and to block pump light and probe light in the DFWM system from entering the optical detector; and measuring an output of the optical detector to represent the DFWM signal. The high spatial resolution of the DFWM in detecting microarray of DNA cells is achieved at such a level to allow for detecting a blank area between two adjacent DNA cells is a feature that is completely missing in any cited portions of the cited McFarland, Mann, Sandstrom and Weinberg.

Therefore, Claim 1 is patentable over the combination of the cited Sandstrom, Weinberg and Tong under 35 USC 103(a).

Turning to Claim 2, based on the above discussion with respect to Claim 1, the combination of the cited Sandstrom, Weinberg and Tong, fails to disclose "scanning the blank area through the DFWM system to measure a signal; and using the measured signal in the blank area to determine a level of hybridization and washing in preparing the DNA cells and background optical noise" in Claim 2.

Claim 3 recites "scanning the position of the microarray to place different locations within a DNA cell in the DFWM system to obtain different DFWM signals from the DNA cell; and using the different DFWM signals from the DNA cell to determine spatial inhomogeniety within the DNA cell." Nothing in the combination of the cited Sandstrom, Weinberg and Tong discloses such features of Claim 3.

Claims 5-7 and 17-22 are patentable based on the above arguments and on their own merits

Therefore, all rejections under 35 USC 103(a) lack support in the contended combination of the cited Sandstrom, Weinberg and Tong. As such, all rejections are improper and must be withdrawn.

Conclusion

In view of the above, all rejections have bee fully addressed and obviated. Therefore, all pending claims are patentable.

The foregoing comments made with respect to the positions taken by the Examiner are not to be construed as acquiescence with other positions of the Examiner that have not been explicitly contested. Accordingly, the above arguments for patentability of a claim should not be construed as implying that there are not other valid reasons for patentability of that claim or other claims.

This response is filed timely with an extension of time for three months. Please apply a fee for the extension of time and any credits or additional charges to deposit account 06-1050.

Respectfully submitted,

Date: November 5, 2009

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